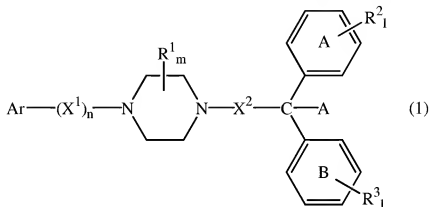


CLAIM AMENDMENTS

1. (currently amended): A method to treat pain which method comprises administering to a subject in need of such treatment an effective amount of a compound of the formula:



or a pharmaceutically acceptable salt thereof,

wherein Ar is phenyl, ~~a six membered or five membered ring which is heteroaromatic or a fused aromatic or heteroaromatic system~~ pyridyl, pyrimidyl, indolyl, benzimidazolyl, benzotriazolyl, isoquinolyl, quinolyl, benzothiazolyl, benzofuranyl, thienyl, furyl, pyrrolyl, thiazolyl, oxazolyl, imidazolyl or phthalimido, each of which may optionally be substituted with one or more ~~non-interfering substituents~~ of alkyl (1-10C), alkenyl (2-10C), alkynyl (2-10C), aryl (6-10C), arylalkyl (1-16C), arylalkenyl (7-16C), each optionally containing 1-4 heteroatoms (N, O or S), O-aryl, O-alkylaryl, O-aroyl, NR-aryl, N-alkylaryl, NR-aroyl, halo, OR, NR₂, SR, -OOCR, -NROCR, RCO, -COOR, -CONR₂, and/or SO₂NR₂, wherein each R is independently H or alkyl (1-8C), and/or by -CN, OCF, -CF₃, and/or NO₂;

~~X¹ is a linker containing 1-5 members~~ 1-5 member chain linking the piperazine to Ar;

n is 1;

~~each R¹-R³ is independently a non-interfering non-hydrogen substituent~~ alkyl (1-10C), alkenyl (2-10C), alkynyl (2-10C), aryl (6-10C), arylalkyl (1-16C), arylalkenyl (7-16C), each optionally containing 1-4 heteroatoms (N, O or S), O-aryl, O-alkylaryl, O-aroyl, NR-aryl, N-alkylaryl, NR-aroyl, halo, OR, NR₂, SR, -OOCR, -NROCR, RCO, -COOR, -CONR₂, and/or

SO<sub>2</sub>NR<sub>2</sub>, wherein each R is independently H or alkyl (1-8C), and/or by -CN, OCF<sub>3</sub>, -CF<sub>3</sub>, and/or NO<sub>2</sub>;

each l is independently 0-5;

m is 0-4;

X<sup>2</sup> is a linker comprising a chain of at least 5 members;

A is H, OR, SR, NR<sub>2</sub>, or halo wherein R is H or lower alkyl (1-6C);

with the proviso that

(a) ~~Ar is a five- or six-membered heteroaryl substituent or an optionally substituted fused aromatic or heteroaromatic substituent~~ pyridyl, pyrimidyl, indolyl, benzimidazolyl, benzotriazolyl, isoquinolyl, quinolyl, benzothiazolyl, benzofuranyl, thienyl, furyl, pyrrolyl, thiazolyl, oxazolyl, imidazolyl or phthalimido optionally substituted with one or more of alkyl (1-10C), alkenyl (2-10C), alkynyl (2-10C), aryl (6-10C), arylalkyl (1-16C), arylalkenyl (7-16C), each optionally containing 1-4 heteroatoms (N, O or S), O-aryl, O-alkylaryl, O-aroyl, NR-aryl, N-alkylaryl, NR-aroyl, halo, OR, NR<sub>2</sub>, SR, -OOCR, -NROCR, RCO, -COOR, -CONR<sub>2</sub>, and/or SO<sub>2</sub>NR<sub>2</sub>, wherein each R is independently H or alkyl (1-8C), and/or by -CN, OCF<sub>3</sub>, and/or NO<sub>2</sub>; and/or

(b) m is 1-4; and/or

(c) X<sup>2</sup> is alkylene substituted by =O, OR, SR, NR<sub>2</sub> and/or halo; and/or

(d) X<sup>2</sup> is a chain of at least 6 members; and/or

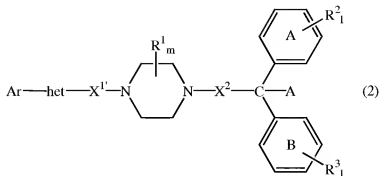
(e) X<sup>2</sup> contains at least one heteroatom selected from N, S and O; and/or

(f) A is OR, SR, NR<sub>2</sub> or halo, wherein R is H or lower alkyl (1-6C) and/or

(g) Ar is substituted with at least one t-butyl moiety or at least one substituted alkoxy; and/or

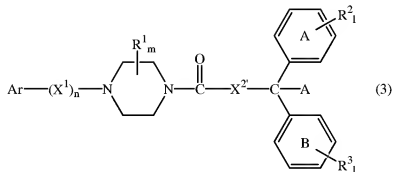
(h) X<sup>1</sup> includes at least one heteroatom selected from O, N and S.

2. (previously presented): The method of claim 1 wherein the compound of formula (1) is of the formula



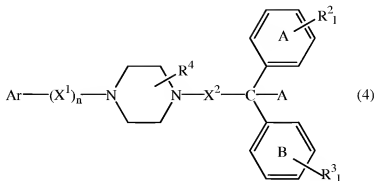
wherein Ar,  $R^1$ - $R^3$ , l, m,  $X^2$  and A are as defined above, "het" is a heteroatom selected from O, S and N, and wherein  $X^{1'}$  is defined as  $X^1$  but lacking one chain member.

3. (previously presented): The method of claim 1 wherein the compound of formula (1) is of the formula



wherein Ar,  $X^1$ ,  $R^1$ - $R^3$ , l, m, n, A and Ar are defined as above, and  $X^{2'}$  is defined as  $X^2$  but lacking one chain member.

4. (previously presented): The method of claim 1 wherein the compound of formula (1) is of the formula



wherein  $R^4$  is =O, or a carboxylic acid group or ester or amide thereof and Ar,  $R^2$ - $R^3$ ,  $X^1$ , 1, n,  $X^2$  and A are defined as above.

5. (currently amended): The method of claim 1, wherein each  $R^1$ - $R^3$  and optional Ar ~~non-interfering~~ substituent is independently alkyl (1-10C), alkenyl (2-10C), alkynyl (2-10C), aryl (6-10C), arylalkyl (7-16C) or arylalkenyl (7-16C) each optionally further containing 1-4 heteroatoms (N, O or S), or is ~~each further optionally substituted, or is independently =O~~, halo,  $CF_3$ , OCF,  $NO_2$ ,  $NH_2$ , OH, or SH wherein S may optionally be oxidized.

6. (canceled)

7. (previously presented): The method of claim 1, wherein each 1 is independently 0 or 1.

8. (canceled)

9. (previously presented): The method of claim 1, wherein  $X^1$  is substituted by =O at the position next to the piperazine ring.

10. (previously presented): The method of claim 1, wherein each of  $R^2$  and  $R^3$  is independently alkoxy, halo, or alkyl.

11. (previously presented): The method of claim 1, wherein m is 1 and R<sup>1</sup> is =O or a is carboxylic acid group or ester or amide thereof.

12. (previously presented): The method of claim 1, wherein Ar is optionally substituted phenyl.

13. (previously presented): The method of claim 12, wherein said phenyl is unsubstituted or is substituted by one or more tert-butyl, methoxy, substituted alkoxy, hydroxy and/or halo.

14. (previously presented): The method of claim 13, wherein the substituted alkoxy is substituted by an amino group.

15. (previously presented): The method of claim 1, wherein Ar is optionally substituted pyrimidyl, pyridyl, benzothiazole, benzimidazole or indole.

16. (previously presented): A method to treat pain which method comprises administering to a subject in need of such treatment an effective amount of a compound selected from the group consisting of

6,6-Bis-(4-fluoro-phenyl)-1-[4-(2-phenylsulfanyl-ethyl)-piperazin-1-yl]-hexan-1-one;  
1-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-4-[2-(4-fluoro-phenoxy)-ethyl]-piperazine;  
1-{4-[2-(Benzo[1,3]dioxol-5-yloxy)-ethyl]-piperazin-1-yl}-6,6-bis-(4-fluoro-phenyl)-hexan-1-one;  
1-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-4-(2-phenylsulfanyl-ethyl)-piperazine;  
1-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-4-[2-(4-methoxy-phenoxy)-ethyl]-piperazine;  
1-{4-[2-(2,4-Difluoro-phenoxy)-ethyl]-piperazin-1-yl}-6,6-bis-(4-fluoro-phenyl)-hexan-1-one;  
6,6-Bis-(4-fluoro-phenyl)-1-[4-(2-phenoxy-ethyl)-piperazin-1-yl]-hexan-1-one;  
1-{4-[2-(2,4-Dichloro-phenoxy)-ethyl]-piperazin-1-yl}-6,6-bis-(4-fluoro-phenyl)-hexan-1-one;

6,6-Bis-(4-fluoro-phenyl)-1-{4-[2-(4-methoxy-phenoxy)-ethyl]-piperazin-1-yl}-hexan-1-one;

1-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-4-(2-phenoxy-ethyl)-piperazine;

6,6-Bis-(4-fluoro-phenyl)-1-{4-[2-(3,4,5-trimethoxy-phenoxy)-ethyl]-piperazin-1-yl}-hexan-1-one;

1-{4-[2-(Benzothiazol-2-ylsulfanyl)-ethyl]-piperazin-1-yl}-6,6-bis-(4-fluoro-phenyl)-hexan-1-one;

[4-(2-{4-[6,6-Bis-(4-fluoro-phenyl)-hexanoyl]-piperazin-1-yl}-ethoxy)-2,3,6-trimethyl-phenyl]-carbamic acid tert-butyl ester;

4-(2-{4-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-piperazin-1-yl}-ethoxy)-2,3,6-trimethyl-phenylamine;

1-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-4-[2-(4-dichloro-phenoxy)-ethyl]-piperazine;

[2-(4-{4-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-piperazin-1-ylmethyl}-2,6-di-tert-butyl-phenoxy)-ethyl]-dimethyl-amine;

4-{4-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-piperazin-1-ylmethyl}-2,6-di-tert-butyl-phenol;

1-[4-(3,5-Di-tert-butyl-4-methoxy-benzoyl)-piperazin-1-yl]-6,6-bis-(4-fluoro-phenyl)-hexan-1-one;

1-[4-(3,5-Di-tert-butyl-4-methoxy-benzyl)-piperazin-1-yl]-6,6-bis-(4-fluoro-phenyl)-hexan-1-one;

1-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-4-(3,5-di-tert-butyl-4-methoxy-benzyl)-piperazine;

{4-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-piperazin-1-yl}-(3,5-di-tert-butyl-4-methoxy-phenyl)-methanone;

1-{4-[3,5-Di-tert-butyl-4-(2-dimethylamino-ethoxy)-benzoyl]-piperazin-1-yl}-6,6-bis-(4-fluoro-phenyl)-hexan-1-one;

1-Benzo[1,3]dioxol-5-ylmethyl-4-[6,6-bis-(4-fluoro-phenyl)-hexyl]-piperazine;

1-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-4-(3,5-di-tert-butyl-benzyl)-piperazine;

{4-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-piperazin-1-yl}-(3,5-di-tert-butyl-4-hydroxy-phenyl)-methanone;

1-[4-(3,5-Di-tert-butyl-4-hydroxy-benzyl)-piperazin-1-yl]-6,6-bis-(4-fluoro-phenyl)-hexan-1-one;

1-[4-(3,5-Dibromo-4-hydroxy-benzoyl)-piperazin-1-yl]-6,6-bis-(4-fluoro-phenyl)-hexan-1-one;

1-[4-(3,5-Di-tert-butyl-4-hydroxy-benzoyl)-piperazin-1-yl]-6,6-bis-(4-fluoro-phenyl)-hexan-1-one;

1-[4-(3,5-Di-tert-butyl-benzoyl)-piperazin-1-yl]-6,6-bis-(4-fluoro-phenyl)-hexan-1-one;

1-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-4-(4-tert-butyl-benzyl)-piperazine;

1-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-4-(9H-thioxanthen-9-yl)-piperazine;

2-{4-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-piperazin-1-yl}-benzothiazole;

6,6-Bis-(4-fluoro-phenyl)-1-(4-pyrimidin-2-yl-piperazin-1-yl)-hexan-1-one;

2-{4-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-piperazin-1-yl}-pyrimidine;

6,6-Bis-(4-fluoro-phenyl)-1-[4-(9H-thioxanthen-9-yl)-piperazin-1-yl]-hexan-1-one;

1-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-4-(3,4,5-trimethoxy-benzyl)-piperazine-2-carboxylic acid ethyl ester;

6,6-Bis-(4-fluoro-phenyl)-1-{4-[2-(3,4,5-trimethoxy-benzylamino)-ethyl]-piperazin-1-yl}-hexan-1-one;

9,9-Bis-(4-fluoro-phenyl)-1-[4-(3,4,5-trimethoxy-benzyl)-piperazin-1-yl]-nonan-1-one;

(2-{4-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-piperazin-1-yl}-ethyl)-phenyl-amine;

1-[9,9-Bis-(4-fluoro-phenyl)-nonyl]-4-(3,4,5-trimethoxy-benzyl)-piperazine;

(4-[4-[Bis-(4-fluoro-phenyl)-methoxy]-butyl]-piperazin-1-yl)-(3,4,5-trimethoxy-phenyl)-methanone;

6,6-Bis-(4-fluoro-phenyl)-1-[4-(4-trifluoromethoxy-benzoyl)-piperazin-1-yl]-hexan-2-one;

1-[4-(4-Bromo-benzoyl)-piperazin-1-yl]-6,6-bis-(4-fluoro-phenyl)-hexan-1-one;

6,6-Bis-(4-fluoro-phenyl)-5-hydroxy-1-[4-(3,4,5-trimethoxy-benzoyl)-piperazin-1-yl]-hexan-1-one;

1-{4-[Bis-(4-fluoro-phenyl)-methoxy]-butyl}-4-(3,4,5-trimethoxy-benzyl)-piperazine;

6,6-Bis-(4-fluoro-phenyl)-6-hydroxy-1-[4-(3,4,5-trimethoxy-benzoyl)-piperazin-1-yl]-hexan-1-one;

4-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-1-(3,4,5-trimethoxy-benzyl)-piperazine-2-carboxylic acid;

4-[6,6-Bis-(4-fluoro-phenyl)-hexanoyl]-1-(3,4,5-trimethoxy-benzyl)-piperazin-2-one;

1-[6,6-Bis-(4-fluoro-phenyl)-hexanoyl]-4-(3,5-di-tert-butyl-4-methoxy-benzoyl)-piperazin-2-one;

1-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-4-(3,4,5-trimethoxy-benzoyl)-piperazin-2-one;

4-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-1-(3,4,5-trimethoxy-benzyl)-piperazin-2-one;

4-[6,6-Bis-(4-fluoro-phenyl)-hexanoyl]-1-(3,5-di-tert-butyl-4-methoxy-benzyl)-piperazin-2-one;

4-[6,6-Bis-(4-fluoro-phenyl)-hexanoyl]-1-[2-(4-fluoro-phenoxy)-ethyl]-piperazin-2-one;

1-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-4-(3,5-di-tert-butyl-4-methoxy-benzoyl)-piperazin-2-one;

4-[6,6-Bis-(4-fluoro-phenyl)-hexanoyl]-1-(3,5-di-tert-butyl-4-methoxy-benzoyl)-piperazin-2-one;

1-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-4-(3,5-di-tert-butyl-4-methoxy-benzoyl)-piperazin-2-one;

1-[6,6-Bis-(4-fluoro-phenyl)-hexanoyl]-4-(3,5-di-tert-butyl-4-hydroxy-benzoyl)-piperazin-2-one;

6,6-Bis-(4-fluoro-phenyl)-1-[4-(3,4,5-trimethoxy-benzoyl)-piperazin-1-yl]-hex-5-en-1-one;

1-[4-[2-(3,4-Dimethoxy-phenoxy)-ethyl]-piperazin-1-yl]-6,6-bis-(4-fluoro-phenyl)-hexan-1-one;

1-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-4-[2-(3,4-dimethoxy-phenoxy)-ethyl]-piperazine;

1-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-4-(3,4,5-trimethoxy-benzyl)-piperazine-2-carboxylic acid;

4-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-1-(3,4,5-trimethoxy-benzyl)-piperazine-2-carboxylic acid ethyl ester;

1-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-4-(3,4-dimethoxy-benzyl)-piperazine;

1-[4-(3,4-Dimethoxy-benzoyl)-piperazin-1-yl]-6,6-bis-(4-fluoro-phenyl)-hexan-1-one;

1-[2-(Benzo[1,3]dioxol-5-yloxy)-ethyl]-4-[6,6-bis-(4-fluoro-phenyl)-hexyl]-piperazine;

1-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-4-[2-(3,4,5-trimethoxy-phenoxy)-ethyl]-piperazine;



1-(4-Amino-2,3,5-trimethyl-phenoxy)-3-{4-[6,6-bis-(4-fluoro-phenyl)-hexyl]-piperazin-1-yl}-propan-2-ol;

1-{4-[3-(4-Amino-2,3,5-trimethyl-phenoxy)-2-hydroxy-propyl]-piperazin-1-yl}-6,6-bis-(4-fluoro-phenyl)-hexan-1-one;

1-(4-Benzothiazol-2-yl)-piperazin-1-yl)-6,6-bis-(4-fluoro-phenyl)-hexan-1-one;

1-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-4-(3,5-bis-trifluoromethyl-benzyl)-piperazine;

1-[4-(3,5-Bis-trifluoromethyl-benzoyl)-piperazin-1-yl]-6,6-bis-(4-fluoro-phenyl)-hexan-1-one;

1-[4-(4-tert-Butyl-benzoyl)-piperazin-1-yl]-6,6-bis-(4-fluoro-phenyl)-hexan-1-one;

1-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-4-(4-bromo-benzyl)-piperazine;

2-(2-{4-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-piperazin-1-yl}-ethylsulfanyl)-benzothiazole;

6,6-Bis-(4-fluoro-phenyl)-1-[4-(4-hydroxy-3,5-dimethoxy-benzoyl)-piperazin-1-yl]-hexan-1-one;

4-{4-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-piperazin-1-ylmethyl}-2,6-dibromo-phenol;

1-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-4-(4-trifluoromethoxy-benzyl)-piperazine;

(2-{4-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-piperazin-1-yl}-ethyl)-(3,4,5-trimethoxy-benzyl)-amine;

1-{4-[2-(4-Fluoro-phenoxy)-ethyl]-piperazin-1-yl}-6,6-bis-(4-fluoro-phenyl)-hexan-1-one;

6,6-Bis-(4-fluoro-phenyl)-1-[4-(2-phenylamino-ethyl)-piperazin-1-yl]-hexan-1-one;

1-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-4-[2-(2,4-difluoro-phenoxy)-ethyl]-piperazine;

N-(2-{4-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-piperazin-1-yl}-2-oxo-ethyl)-benzamide;

N-(2-{4-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-piperazin-1-yl}-2-oxo-ethyl)-4-chloro-benzamide;

N-(2-{4-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-piperazin-1-yl}-2-oxo-ethyl)-4-methyl-benzamide;

N-(2-{4-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-piperazin-1-yl}-2-oxo-ethyl)-4-isopropyl-benzamide;

N-(2-{4-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-piperazin-1-yl}-2-oxo-ethyl)-4-tert-butyl-benzamide;

N-(2-{4-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-piperazin-1-yl}-2-oxo-ethyl)-4-fluoro-benzamide;

N-(2-{4-[6,6-Bis-(4-fluoro-phenyl)-hexanoyl]-piperazin-1-yl}-2-oxo-ethyl)-benzamide;

N-(2-{4-[6,6-Bis-(4-fluoro-phenyl)-hexanoyl]-piperazin-1-yl}-2-oxo-ethyl)-4-chloro-benzamide;

N-(2-{4-[6,6-Bis-(4-fluoro-phenyl)-hexanoyl]-piperazin-1-yl}-2-oxo-ethyl)-4-methyl-benzamide;

N-(2-{4-[6,6-Bis-(4-fluoro-phenyl)-hexanoyl]-piperazin-1-yl}-2-oxo-ethyl)-4-isopropyl-benzamide;

N-(2-{4-[6,6-Bis-(4-fluoro-phenyl)-hexanoyl]-piperazin-1-yl}-2-oxo-ethyl)-4-tert-butyl-benzamide;

N-(2-{4-[6,6-Bis-(4-fluoro-phenyl)-hexanoyl]-piperazin-1-yl}-2-oxo-ethyl)-4-fluoro-benzamide;

1-[4-(2-Benzylamino-ethyl)-piperazin-1-yl]-6,6-bis-(4-fluoro-phenyl)-hexan-1-one;

1-{4-[2-(4-Chloro-benzylamino)-ethyl]-piperazin-1-yl}-6,6-bis-(4-fluoro-phenyl)-hexan-1-one;

6,6-Bis-(4-fluoro-phenyl)-1-{4-[2-(4-methyl-benzylamino)-ethyl]-piperazin-1-yl}-hexan-1-one;

6,6-Bis-(4-fluoro-phenyl)-1-{4-[2-(4-isopropyl-benzylamino)-ethyl]-piperazin-1-yl}-hexan-1-one;

1-{4-[2-(4-tert-Butyl-benzylamino)-ethyl]-piperazin-1-yl}-6,6-bis-(4-fluoro-phenyl)-hexan-1-one;

1-{4-[2-(4-Fluoro-benzylamino)-ethyl]-piperazin-1-yl}-6,6-bis-(4-fluoro-phenyl)-hexan-1-one;

6,6-Bis-(4-fluoro-phenyl)-1-[4-(1-hydroxy-pyridine-4-carbonyl)-piperazin-1-yl]-hexan-1-one;

4-{4-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-piperazin-1-ylmethyl}-2,6-dimethoxy-phenol;

9,9-Diphenyl-1-[4-(3,4,5-trimethoxy-benzyl)-piperazin-1-yl]-nonan-1-one;

1-[4-(3,5-Di-tert-butyl-4-methoxy-benzoyl)-2-methyl-piperazin-1-yl]-6,6-bis-(4-fluoro-phenyl)-hexan-1-one;

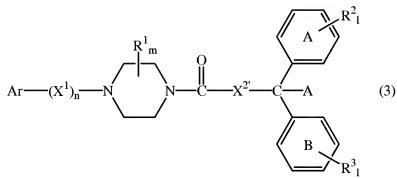
1-[4-(3,5-Di-tert-butyl-4-methoxy-benzoyl)-3-methyl-piperazin-1-yl]-6,6-bis-(4-fluoro-phenyl)-hexan-1-one;

1-[4-(3,5-Di-tert-butyl-benzoyl)-2-methyl-piperazin-1-yl]-6,6-bis-(4-fluoro-phenyl)-hexan-1-one; and

1-[4-(4-tert-Butyl-benzoyl)-2-methyl-piperazin-1-yl]-6,6-bis-(4-fluoro-phenyl)-hexan-1-one, including the pharmaceutically acceptable salts thereof.

17-18. (canceled)

19. (currently amended): A compound of the formula



wherein Ar is phenyl, ~~a six membered or five membered ring which is heteroaromatic or a fused aromatic or heteroaromatic system~~ pyridyl, pyrimidyl, indolyl, benzimidazolyl, benzotriazolyl, isoquinolyl, quinolyl, benzothiazolyl, benzofuranyl, thienyl, furyl, pyrrolyl, thiazolyl, oxazolyl, imidazolyl or phthalimido, each of which may optionally be substituted with one or more ~~non interfering substituents~~ alkyl (1-10C), alkenyl (2-10C), alkynyl (2-10C), aryl (6-10C), arylalkyl (1-16C), arylalkenyl (7-16C), each optionally containing 1-4 heteroatoms (N, O or S), O-aryl, O-alkylaryl, O-aryl, NR-aryl, N-alkylaryl, NR-aryl, halo, OR, NR<sub>2</sub>, SR, -OOCR, -NROCR, RCO, -COOR, -CONR<sub>2</sub>, and/or SO<sub>2</sub>NR<sub>2</sub>, wherein each R is independently H or alkyl (1-8C), and/or by -CN, OCF, -CF<sub>3</sub>, and/or NO<sub>2</sub>;

X<sup>1</sup> is ~~a linker containing 1-5 members~~ 1-5 member chain linking the piperazine to Ar;

n is 1;

each  $R^1$ - $R^3$  is independently a ~~non-interfering non-hydrogen substituent~~ alkyl (1-10C), alkenyl (2-10C), alkynyl (2-10C), aryl (6-10C), arylalkyl (1-16C), arylalkenyl (7-16C), each optionally containing 1-4 heteroatoms (N, O or S), O-aryl, O-alkylaryl, O-aroyle, NR-aryl, N-alkylaryl, NR-aroyle, halo, OR,  $NR_2$ , SR, -OOCR, -NROCR, RCO, -COOR, -CONR<sub>2</sub>, and/or SO<sub>2</sub>NR<sub>2</sub>, wherein each R is independently H or alkyl (1-8C), and/or by -CN, OCF, -CF<sub>3</sub>, and/or NO<sub>2</sub>;

each l is independently 0-5;

m is 0-4;

$X^{2'}$  is a linker comprising a chain of at least 4 members;

A is H, OR, SR, NR<sub>2</sub>, or halo wherein R is H or lower alkyl (1-6C);

with the proviso that

(a) Ar is a ~~five- or six-membered heteroaryl substituent or an optionally substituted fused aromatic or heteroaromatic substituent~~ pyridyl, pyrimidyl, indolyl, benzimidazolyl, benzotriazolyl, isoquinolyl, quinolyl, benzothiazolyl, benzofuranyl, thienyl, furyl, pyrrolyl, thiazolyl, oxazolyl, imidazolyl or phthalimido optionally substituted with one or more of alkyl (1-10C), alkenyl (2-10C), alkynyl (2-10C), aryl (6-10C), arylalkyl (1-16C), arylalkenyl (7-16C), each optionally containing 1-4 heteroatoms (N, O or S), O-aryl, O-alkylaryl, O-aroyle, NR-aryl, N-alkylaryl, NR-aroyle, halo, OR,  $NR_2$ , SR, -OOCR, -NROCR, RCO, -COOR, -CONR<sub>2</sub>, and/or SO<sub>2</sub>NR<sub>2</sub>, wherein each R is independently H or alkyl (1-8C), and/or by -CN, OCF, -CF<sub>3</sub>, and/or NO<sub>2</sub>; and/or

(b) m is 1-4; and/or

(c)  $X^2$  is alkylene substituted by =O, OR, SR, NR<sub>2</sub> and/or halo; and/or

(d)  $X^2$  is a chain of at least 6 members; and/or

(e)  $X^2$  contains at least one heteroatom selected from N, S and O; and/or

(f) A is OR, SR, NR<sub>2</sub> or halo, wherein R is H or lower alkyl (1-6C) and/or

(g) Ar is substituted with at least one t-butyl moiety or at least one substituted alkoxy; and/or

(h)  $X^1$  includes at least one heteroatom selected from O, N and S.

20. (currently amended): The compound of claim 19, wherein each  $R^1$ - $R^3$  and optional ~~Ar non-interfering~~ substituent is independently alkyl (1-10C), alkenyl (2-10C), alkynyl (2-10C), aryl (6-10C), arylalkyl (7-16C) or arylalkenyl (7-16C) each optionally further containing 1-4 heteroatoms (N, O or S) ~~each further optionally substituted~~, or is independently  $[=O]$ , halo,  $CF_3$ , OCF,  $NO_2$ ,  $NH_2$ , OH, or SH wherein S may optionally be oxidized.

21. (previously presented): The compound of claim 19, wherein each l is independently 0 or 1.

22. (previously presented): The compound of claim 19, wherein  $X^1$  is substituted by =O at the position next to the piperazine ring.

23. (previously presented): The compound of claim 19, wherein each of  $R^2$  and  $R^3$  is independently alkoxy, halo, or alkyl.

24. (previously presented): The compound of claim 19, wherein m is 1 and  $R^1$  is =O or a carboxylic acid group or ester or amide thereof.

25. (previously presented): The compound of claim 19, wherein Ar is optionally substituted phenyl.

26. (previously presented): The compound of claim 25, wherein said phenyl is unsubstituted or is substituted by one or more tert-butyl, methoxy, substituted alkoxy, hydroxy and/or halo.

27. (previously presented): The compound of claim 26, wherein the substituted alkoxy is substituted by an amino group.

28. (previously presented): The compound of claim 19, wherein Ar is optionally substituted pyrimidyl, pyridyl, benzothiazole, benzimidazole or indole.

29. (previously presented): A compound selected from the group consisting of

6,6-Bis-(4-fluoro-phenyl)-1-[4-(2-phenylsulfanyl-ethyl)-piperazin-1-yl]-hexan-1-one;

1-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-4-[2-(4-fluoro-phenoxy)-ethyl]-piperazine;

1-{4-[2-(Benzo[1,3]dioxol-5-yloxy)-ethyl]-piperazin-1-yl}-6,6-bis-(4-fluoro-phenyl)-hexan-1-one;

1-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-4-(2-phenylsulfanyl-ethyl)-piperazine;

1-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-4-[2-(4-methoxy-phenoxy)-ethyl]-piperazine;

1-{4-[2-(2,4-Difluoro-phenoxy)-ethyl]-piperazin-1-yl}-6,6-bis-(4-fluoro-phenyl)-hexan-1-one;

6,6-Bis-(4-fluoro-phenyl)-1-[4-(2-phenoxy-ethyl)-piperazin-1-yl]-hexan-1-one;

1-{4-[2-(2,4-Dichloro-phenoxy)-ethyl]-piperazin-1-yl}-6,6-bis-(4-fluoro-phenyl)-hexan-1-one;

6,6-Bis-(4-fluoro-phenyl)-1-{4-[2-(4-methoxy-phenoxy)-ethyl]-piperazin-1-yl}-hexan-1-one;

1-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-4-(2-phenoxy-ethyl)-piperazine;

6,6-Bis-(4-fluoro-phenyl)-1-{4-[2-(3,4,5-trimethoxy-phenoxy)-ethyl]-piperazin-1-yl}-hexan-1-one;

1-{4-[2-(Benzothiazol-2-ylsulfanyl)-ethyl]-piperazin-1-yl}-6,6-bis-(4-fluoro-phenyl)-hexan-1-one;

[4-(2-{4-[6,6-Bis-(4-fluoro-phenyl)-hexanoyl]-piperazin-1-yl}-ethoxy)-2,3,6-trimethyl-phenyl]-carbamic acid tert-butyl ester;

4-(2-{4-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-piperazin-1-yl}-ethoxy)-2,3,6-trimethyl-phenylamine;

1-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-4-[2-(2,4-dichloro-phenoxy)-ethyl]-piperazine;

[2-(4-{4-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-piperazin-1-ylmethyl}-2,6-di-tert-butyl-phenoxy)-ethyl]-dimethyl-amine;

4-{4-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-piperazin-1-ylmethyl}-2,6-di-tert-butyl-phenol;

1-[4-(3,5-Di-tert-butyl-4-methoxy-benzoyl)-piperazin-1-yl]-6,6-bis-(4-fluoro-phenyl)-hexan-1-one;

1-[4-(3,5-Di-tert-butyl-4-methoxy-benzyl)-piperazin-1-yl]-6,6-bis-(4-fluoro-phenyl)-hexan-1-one;

1-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-4-(3,5-di-tert-butyl-4-methoxy-benzyl)-piperazine;  
{4-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-piperazin-1-yl}-(3,5-di-tert-butyl-4-methoxy-phenyl)-methanone;

1-{4-[3,5-Di-tert-butyl-4-(2-dimethylamino-ethoxy)-benzoyl]-piperazin-1-yl}-6,6-bis-(4-fluoro-phenyl)-hexan-1-one;

1-Benzo[1,3]dioxol-5-ylmethyl-4-[6,6-bis-(4-fluoro-phenyl)-hexyl]-piperazine;  
1-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-4-(3,5-di-tert-butyl-benzyl)-piperazine;  
{4-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-piperazin-1-yl}-(3,5-di-tert-butyl-4-hydroxy-phenyl)-methanone;

1-[4-(3,5-Di-tert-butyl-4-hydroxy-benzyl)-piperazin-1-yl]-6,6-bis-(4-fluoro-phenyl)-hexan-1-one;

1-[4-(3,5-Dibromo-4-hydroxy-benzoyl)-piperazin-1-yl]-6,6-bis-(4-fluoro-phenyl)-hexan-1-one;

1-[4-(3,5-Di-tert-butyl-4-hydroxy-benzoyl)-piperazin-1-yl]-6,6-bis-(4-fluoro-phenyl)-hexan-1-one;

1-[4-(3,5-Di-tert-butyl-benzoyl)-piperazin-1-yl]-6,6-bis-(4-fluoro-phenyl)-hexan-1-one;  
1-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-4-(4-tert-butyl-benzyl)-piperazine;  
1-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-4-(9H-thioxanthen-9-yl)-piperazine;  
2-{4-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-piperazin-1-yl}-benzothiazole;  
6,6-Bis-(4-fluoro-phenyl)-1-(4-pyrimidin-2-yl-piperazin-1-yl)-hexan-1-one;  
2-{4-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-piperazin-1-yl}-pyrimidine;  
6,6-Bis-(4-fluoro-phenyl)-1-[4-(9H-thioxanthen-9-yl)-piperazin-1-yl]-hexan-1-one;  
1-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-4-(3,4,5-trimethoxy-benzyl)-piperazine-2-carboxylic acid ethyl ester;

6,6-Bis-(4-fluoro-phenyl)-1-{4-[2-(3,4,5-trimethoxy-benzylamino)-ethyl]-piperazin-1-yl}-hexan-1-one;

9,9-Bis-(4-fluoro-phenyl)-1-[4-(3,4,5-trimethoxy-benzyl)-piperazin-1-yl]-nonan-1-one;

(2-[4-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-piperazin-1-yl]-ethyl)-phenyl-amine;  
1-[9,9-Bis-(4-fluoro-phenyl)-nonyl]-4-(3,4,5-trimethoxy-benzyl)-piperazine;  
4-[4-[Bis-(4-fluoro-phenyl)-methoxy]-butyl]-piperazin-1-yl)-(3,4,5-trimethoxy-phenyl)-methanone;  
6,6-Bis-(4-fluoro-phenyl)-1-[4-(4-trifluoromethoxy-benzoyl)-piperazin-1-yl]-hexan-2-one;  
1-[4-(4-Bromo-benzoyl)-piperazin-1-yl]-6,6-bis-(4-fluoro-phenyl)-hexan-1-one;  
6,6-Bis-(4-fluoro-phenyl)-5-hydroxy-1-[4-(3,4,5-trimethoxy-benzoyl)-piperazin-1-yl]-hexan-1-one;  
1-[4-[Bis-(4-fluoro-phenyl)-methoxy]-butyl]-4-(3,4,5-trimethoxy-benzyl)-piperazine;  
6,6-Bis-(4-fluoro-phenyl)-6-hydroxy-1-[4-(3,4,5-trimethoxy-benzoyl)-piperazin-1-yl]-hexan-1-one;  
4-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-1-(3,4,5-trimethoxy-benzyl)-piperazine-2-carboxylic acid;  
4-[6,6-Bis-(4-fluoro-phenyl)-hexanoyl]-1-(3,4,5-trimethoxy-benzyl)-piperazin-2-one;  
1-[6,6-Bis-(4-fluoro-phenyl)-hexanoyl]-4-(3,5-di-tert-butyl-4-methoxy-benzoyl)-piperazin-2-one;  
1-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-4-(3,4,5-trimethoxy-benzoyl)-piperazin-2-one;  
4-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-1-(3,4,5-trimethoxy-benzyl)-piperazin-2-one;  
4-[6,6-Bis-(4-fluoro-phenyl)-hexanoyl]-1-(3,5-di-tert-butyl-4-methoxy-benzyl)-piperazin-2-one;  
4-[6,6-Bis-(4-fluoro-phenyl)-hexanoyl]-1-[2-(4-fluoro-phenoxy)-ethyl]-piperazin-2-one;  
1-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-4-(3,5-di-tert-butyl-4-methoxy-benzoyl)-piperazin-2-one;  
4-[6,6-Bis-(4-fluoro-phenyl)-hexanoyl]-1-(3,5-di-tert-butyl-4-methoxy-benzoyl)-piperazin-2-one;  
1-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-4-(3,5-di-tert-butyl-4-methoxy-benzyl)-piperazin-2-one;  
1-[6,6-Bis-(4-fluoro-phenyl)-hexanoyl]-4-(3,5-di-tert-butyl-4-hydroxy-benzoyl)-piperazin-2-one;  
6,6-Bis-(4-fluoro-phenyl)-1-[4-(3,4,5-trimethoxy-benzoyl)-piperazin-1-yl]-hex-5-en-1-one;



1-[4-[2-(3,4-Dimethoxy-phenoxy)-ethyl]-piperazin-1-yl]-6,6-bis-(4-fluoro-phenyl)-hexan-1-one;

1-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-4-[2-(3,4-dimethoxy-phenoxy)-ethyl]-piperazine;

1-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-4-(3,4,5-trimethoxy-benzyl)-piperazine-2-carboxylic acid;

4-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-1-(3,4,5-trimethoxy-benzyl)-piperazine-2-carboxylic acid ethyl ester;

1-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-4-(3,4-dimethoxy-benzyl)-piperazine;

1-[4-(3,4-Dimethoxy-benzoyl)-piperazin-1-yl]-6,6-bis-(4-fluoro-phenyl)-hexan-1-one;

1-[2-(Benzo[1,3]dioxol-5-yloxy)-ethyl]-4-[6,6-bis-(4-fluoro-phenyl)-hexyl]-piperazine;

1-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-4-[2-(3,4,5-trimethoxy-phenoxy)-ethyl]-piperazine;

1-(4-Amino-2,3,5-trimethyl-phenoxy)-3-{4-[6,6-bis-(4-fluoro-phenyl)-hexyl]-piperazin-1-yl}-propan-2-ol;

1-[4-[3-(4-Amino-2,3,5-trimethyl-phenoxy)-2-hydroxy-propyl]-piperazin-1-yl]-6,6-bis-(4-fluoro-phenyl)-hexan-1-one;

1-(4-Benzothiazol-2-yl)-piperazin-1-yl]-6,6-bis-(4-fluoro-phenyl)-hexan-1-one;

1-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-4-(3,5-bis-trifluoromethyl-benzyl)-piperazine;

1-[4-(3,5-Bis-trifluoromethyl-benzoyl)-piperazin-1-yl]-6,6-bis-(4-fluoro-phenyl)-hexan-1-one;

1-[4-(4-tert-Butyl-benzoyl)-piperazin-1-yl]-6,6-bis-(4-fluoro-phenyl)-hexan-1-one;

1-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-4-(4-bromo-benzyl)-piperazine;

2-(2-[4-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-piperazin-1-yl]-ethylsulfanyl)-benzothiazole;

6,6-Bis-(4-fluoro-phenyl)-1-[4-(4-hydroxy-3,5-dimethoxy-benzoyl)-piperazin-1-yl]-hexan-1-one;

4-{4-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-piperazin-1-ylmethyl}-2,6-dibromo-phenol;

1-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-4-(4-trifluoromethoxy-benzyl)-piperazine;

(2-[4-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-piperazin-1-yl]-ethyl)-(3,4,5-trimethoxy-benzyl)-amine;

1-[4-[2-(4-Fluoro-phenoxy)-ethyl]-piperazin-1-yl]-6,6-bis-(4-fluoro-phenyl)-hexan-1-one;

6,6-Bis-(4-fluoro-phenyl)-1-[4-(2-phenylamino-ethyl)-piperazin-1-yl]-hexan-1-one;  
1-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-4-[2-(2,4-difluoro-phenoxy)-ethyl]-piperazine;  
N-(2-{4-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-piperazin-1-yl}-2-oxo-ethyl)-benzamide;  
N-(2-{4-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-piperazin-1-yl}-2-oxo-ethyl)-4-chloro-  
benzamide;

N-(2-{4-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-piperazin-1-yl}-2-oxo-ethyl)-4-methyl-  
benzamide;

N-(2-{4-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-piperazin-1-yl}-2-oxo-ethyl)-4-isopropyl-  
benzamide;

N-(2-{4-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-piperazin-1-yl}-2-oxo-ethyl)-4-tert-butyl-  
benzamide;

N-(2-{4-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-piperazin-1-yl}-2-oxo-ethyl)-4-fluoro-  
benzamide;

N-(2-{4-[6,6-Bis-(4-fluoro-phenyl)-hexanoyl]-piperazin-1-yl}-2-oxo-ethyl)-benzamide;

N-(2-{4-[6,6-Bis-(4-fluoro-phenyl)-hexanoyl]-piperazin-1-yl}-2-oxo-ethyl)-4-chloro-  
benzamide;

N-(2-{4-[6,6-Bis-(4-fluoro-phenyl)-hexanoyl]-piperazin-1-yl}-2-oxo-ethyl)-4-methyl-  
benzamide;

N-(2-{4-[6,6-Bis-(4-fluoro-phenyl)-hexanoyl]-piperazin-1-yl}-2-oxo-ethyl)-4-isopropyl-  
benzamide;

N-(2-{4-[6,6-Bis-(4-fluoro-phenyl)-hexanoyl]-piperazin-1-yl}-2-oxo-ethyl)-4-tert-butyl-  
benzamide;

N-(2-{4-[6,6-Bis-(4-fluoro-phenyl)-hexanoyl]-piperazin-1-yl}-2-oxo-ethyl)-4-fluoro-  
benzamide;

1-[4-(2-Benzylamino-ethyl)-piperazin-1-yl]-6,6-bis-(4-fluoro-phenyl)-hexan-1-one;

1-{4-[2-(4-Chloro-benzylamino)-ethyl]-piperazin-1-yl}-6,6-bis-(4-fluoro-phenyl)-  
hexan-1-one;

6,6-Bis-(4-fluoro-phenyl)-1-{4-[2-(4-methyl-benzylamino)-ethyl]-piperazin-1-yl}-  
hexan-1-one;

6,6-Bis-(4-fluoro-phenyl)-1-[4-[2-(4-isopropyl-benzylamino)-ethyl]-piperazin-1-yl]-hexan-1-one;

1-[4-[2-(4-tert-Butyl-benzylamino)-ethyl]-piperazin-1-yl]-6,6-bis-(4-fluoro-phenyl)-hexan-1-one;

1-[4-[2-(4-Fluoro-benzylamino)-ethyl]-piperazin-1-yl]-6,6-bis-(4-fluoro-phenyl)-hexan-1-one;

6,6-Bis-(4-fluoro-phenyl)-1-[4-(1-hydroxy-pyridine-4-carbonyl)-piperazin-1-yl]-hexan-1-one;

4-[4-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-piperazin-1-ylmethyl]-2,6-dimethoxy-phenol;

9,9-Diphenyl-1-[4-(3,4,5-trimethoxy-benzyl)-piperazin-1-yl]-nonan-1-one;

1-[4-(3,5-Di-tert-butyl-4-methoxy-benzoyl)-2-methyl-piperazin-1-yl]-6,6-bis-(4-fluoro-phenyl)-hexan-1-one;

1-[4-(3,5-Di-tert-butyl-4-methoxy-benzoyl)-3-methyl-piperazin-1-yl]-6,6-bis-(4-fluoro-phenyl)-hexan-1-one;

1-[4-(3,5-Di-tert-butyl-benzoyl)-2-methyl-piperazin-1-yl]-6,6-bis-(4-fluoro-phenyl)-hexan-1-one; and

1-[4-(4-tert-Butyl-benzoyl)-2-methyl-piperazin-1-yl]-6,6-bis-(4-fluoro-phenyl)-hexan-1-one, including the pharmaceutically acceptable salts thereof.

30. (previously presented): A pharmaceutical composition which comprises, in admixture with a pharmaceutically acceptable excipient, a unit dosage amount of at least one compound of claim 19.

31. (previously presented): A pharmaceutical composition which comprises, in admixture with a pharmaceutically acceptable excipient, a unit dosage amount of at least one compound of claim 29.